OPINION

The vortex—an early predictor of cardiovascular outcome?

Gianni Pedrizzetti, Giovanni La Canna, Ottavio Alfieri and Giovanni Tonti

Abstract | Blood motion in the heart features vortices that accompany the redirection of jet flows towards the outlet tracks. Vortices have a crucial role in fluid dynamics. The stability of cardiac vorticity is vital to the dynamic balance between rotating blood and myocardial tissue and to the development of cardiac dysfunction. Moreover, vortex dynamics immediately reflect physiological changes to the surrounding system, and can provide early indications of long-term outcome. However, the pathophysiological relevance of cardiac fluid dynamics is still unknown. We postulate that maladaptive intracardiac vortex dynamics might modulate the progressive remodelling of the left ventricle towards heart failure. The evaluation of blood flow presents a new paradigm in cardiac function analysis, with the potential for sensitive risk identification of cardiac abnormalities. Description of cardiac flow patterns after surgery or device therapy provides an intrinsic qualitative evaluation of therapeutic procedures, and could enable early risk stratification of patients vulnerable to adverse cardiac remodelling.

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Introduction

A distinguishing feature of cardiac blood flow is the presence of vortices,[1,2] which are ring-shaped regions of rotating flow motion. Vortices are well-known entities in fluid dynamics, characterized by instability that can markedly influence mechanical function. The process of developing clinical indicators on the basis of cardiac blood flow must differ from the process used to generate clinical indicators for tissue deformation. For example, although wall motion abnormalities, such as hypokinesia or asynchrony, directly indicate the existence of overt clinical disease, abnormal left ventricular (LV) flow patterns could signal the presence of a maladaptive function even before noticeable structural changes arise. Flow analysis might, therefore, reveal preclinical disease or physiologically unstable conditions that can trigger the sequence of events leading to progressive LV remodelling and clinically overt heart failure.

Imaging is used in the clinical setting to evaluate LV function in terms of volume change and cardiac output (the heart as a volumetric pump). With the use of imaging techniques developed over the past 10 years, such as myocardial strain and speckle tracking, the characterization of LV function in terms of muscular deformation (the heart as a muscular pump) has become possible. In this context, research into the properties of blood flow inside the cardiac cavities has been restricted to Doppler assessment of the heart valves,[3] or to the description of the pulsed wave patterns at the mitral inlet.[4] The evaluation of blood flow might pave the way for new cardiac function analysis, resulting in highly sensitive identification of cardiac abnormalities. This assessment of blood flow would involve a multidisciplinary approach, combining an understanding of the physics involved in LV function with the exploitation of available imaging technology, while maintaining the focus on the clinical applications of these analyses.

Although the pathophysiological relevance of cardiac fluid dynamics is still unknown and quantitative data are lacking, we believe that maladaptive intracardiac vortices might be involved in the complex pathway that triggers and modulates LV remodelling. In this Perspectives article, we examine cardiac vortex flow as a sensitive pathogenic indicator and modulator of cardiac LV remodelling towards heart failure. Analysing abnormalities in fluid dynamics that either precede, or are an unfavourable consequence of, overt heart disease can provide a new paradigm in the assessment of cardiovascular diagnosis and outcome. In addition, we suggest that analysis of cardiac blood flow patterns after cardiac surgery or device therapy could optimize qualitative postprocedural evaluation, and permit early risk stratification of patients vulnerable to adverse cardiac remodelling and related outcomes.

The physics of vortex dynamics

LV function is based on a complex muscle-pump system that achieves adequate stroke volume without an increase in filling pressure (at rest and during exercise). This model of ejection based on low-pressure filling requires interplay between the anatomical helical arrangement of myocardial fibres and the physiological processes of excitation, contraction, and relaxation.[5–8] New imaging techniques, such as MRI myocardial tagging[9] and MRI diffusion tensor,[10] have provided comprehensive quantitative analysis of the interplay between structure and function in cardiac mechanics. The isovolumic relaxation rate, together with an untwisting feature, enhance the elastic recoil of potential energy stored in the myocardium during the contraction phase, supporting the decline in intraventricular pressure gradients (IVPG) and generating an active apical suction force.[11,12] Consequently, LV filling is facilitated by suction without the 'pushing' increase of left atrial pressure. Although IVPG analysis can characterize filling haemodynamics,[13] this technique is not appropriate in clinical practice owing to its invasiveness and complexity. Analysis of intracavity flow characteristics with either phase-contrast cardiac MRI (PCMR) or echocardiographic methods is a noninvasive approach to evaluating LV filling–ejection dynamics, adding new concepts to the conventional muscle-pump model that is primarily based on indices of wall mechanics.[14]

Blood flow dynamics in the left ventricle feature the formation of vortices[1,2] associated with the smooth redirection of flow from the inlet to the outflow tract. The vortex is necessary for regular filling-to-ejection transition. The typical pattern of blood flow in a

Competing interests
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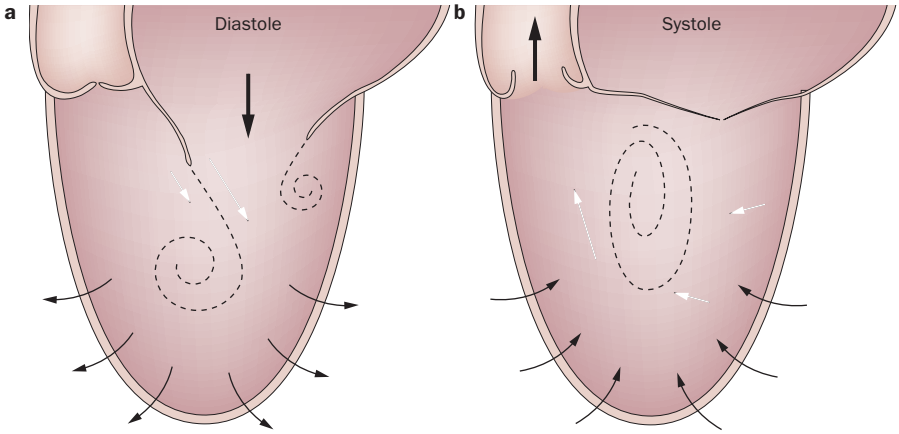

Figure 1 | Blood flow in the healthy left ventricle. **a** | Blood flows into the left ventricle during diastole (thick black arrow), propelled by base-to-apex pressure gradients (thin black arrows). Blood develops a shear layer at the trailing edge of the anterior mitral leaflet, owing to different blood velocities on the two sides of the leaflet (white arrows). The shear layer is transported inside the cavity and rolls up into a vortex. At the end of diastole, the vortex provides circulation of blood (clockwise, in this view) that redirects the inflow of blood towards the outflow tract. **b** | At the onset of systole, the pressure gradient is directed from the apex to the base (thin black arrows) and the rotating flow converges from the cavity towards the aorta (white arrows). The vortex naturally accompanies the transformation of incoming downward-directed flow into upward outflow (thick black arrow).

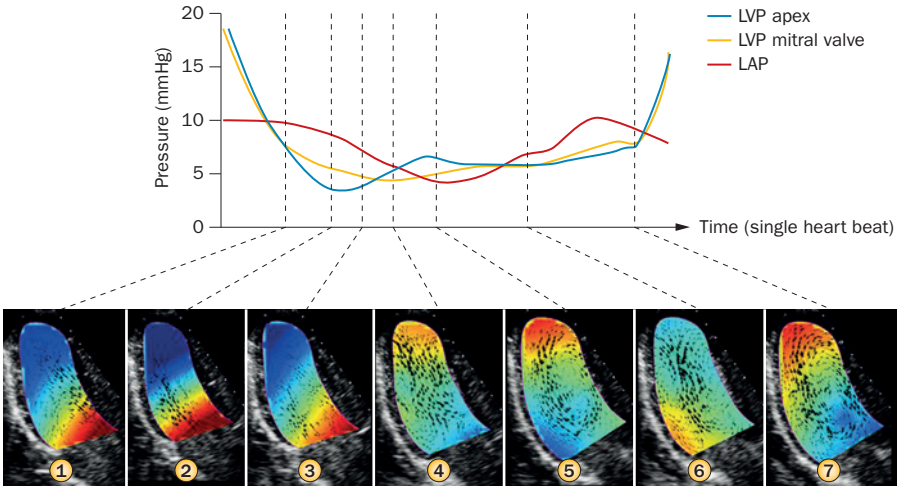

Figure 2 | Time profile of pressure in healthy left cardiac chambers. Time profile of LVP at the apex and at the level of the mitral valve, and of LAP, with corresponding left ventricular blood motion and pressure gradient maps. At the end of systole (image 1), pressure is higher at the base than at the apex and decelerates outgoing blood until the early filling phase (images 2 and 3) in which blood accelerates from the mitral orifice into the ventricular chamber and creates the vortex. Owing to ongoing relaxation, the left ventricle enlarges causing a global pressure drop within the heart, with a lower pressure at the apex than the base. The pressure gradient reaches the apex triggering a rapid increase in the apical LVP and, when the flow decelerates, the vortex ring then smoothly sets in the middle of the expanding ventricle (image 5). During the slow filling phase (image 6), the difference between the pressure at the apex and the base reduces. At the end of diastole (image 7), blood circulation almost effortlessly accomplishes the physiological flow redirection from the inlet to the outflow tract; the pre-ejection reversal of the pressure gradient, from apex to base, decelerates the incoming fluid and accelerates the outgoing flow towards the aortic outlet, smoothly transforming the intracavity rotation into an ejection. Blue indicates low pressure and red indicates high pressure. Abbreviations: LAP, left atrial pressure; LVP, left ventricular pressure.

healthy left ventricle is shown in Figure 1. During the rapid filling phase, blood enters through the mitral orifice and develops a shear layer (a layer separating two regions with different velocities characterized by high shear friction) at the trailing edges of the valve, particularly the anterior leaflet. This shear layer is transported inside the LV cavity towards the apex and 'rolls up' into a vortex. Initially, the apical region has a lower pressure than the base of the heart; after peak velocity, the pressure gradient progressively reverses until pressure at the apex exceeds that at the base, decelerating the incoming blood while the vortex travels smoothly towards the middle of the left ventricle.[15–18] At the end of diastole, blood circulates posteriorly from the base to the apex and anteriorly from the apex to the base, and is thus redirected from the inlet to the outflow tract. During the pre-ejection phase, the pressure gradient, pushing from apex to base, decelerates the incoming fluid and accelerates the outflow towards the aorta, smoothly transforming the intracavity rotation into an ejection process (Figure 2).

Vortices modulate energy transformation and momentum transfer. They are dynamic structures, characterized by an intrinsic instability, giving rise to rapid acceleration, deviations, and sharp fluctuations in pressure and shear stress. In the absence of vortices, blood flow is intuitive and predictable. The instability of vortices also leads to an easy loss of coherence, turbulence, and breaking up into small, irregular vortex structures. The presence of vortices in blood motion suggests that minor modifications in the surrounding conditions can lead to large differences in energetic or dynamic properties, changing the balance between flowing blood and cardiac tissue.

Imaging of LV fluid dynamics

Diagnostic cardiovascular imaging has undergone rapid advances during the past 2 decades, with research focusing mainly on the visualization of tissue elements. However, techniques for the evaluation of cardiac fluid dynamics have been developed only during the past 10 years. The main features of normal intraventricular flow organization have been characterized using various imaging techniques.[14]

PCMR can be used to provide details of the 3D flow field.[19] The application of this modality to intraventricular flow allows quantification of vortical properties in terms of fluid dynamics, although research in this field is mostly centred on flow transit properties.[20–22] In addition to the known technical limitations (low space and time resolution, information averaged over a large number of heart beats, and not being applicable in the presence of implanted cardiac devices), PCMR has the disadvantage of substantial technical complexity and

high costs for routine clinical practice. This technique cannot be used intraoperatively, or in patients with cardiac devices in whom echocardiography remains the only option. Consequently, in this Perspectives article, we do not provide a detailed analysis of PCMR in vortex evaluation owing to its limited application in the context of large, population-based studies.

3D Doppler echocardiography is not adequate to detect vortex structures because it measures only one component of the velocity vector, and does not evaluate directional change or velocity gradients. An echocardiographic technique utilizing B-mode harmonic imaging can be used to evaluate instantaneous vortical blood motion in the left ventricle. A patient is given a low-dose intravenous injection of ultrasound microbubble contrast agent that has the same rheological behaviour as red blood cells and can be considered a blood flow tracer. Such bubbles visually display swirling intracardiac motion, and images can be processed by an echocardiographic adaptation of the particle image velocimetry (PIV) technology ('echo-PIV'), which has long been used in fluid dynamics laboratories.[23] The echo-PIV concept has been validated *in vitro* in comparison with laser-based digital PIV.[24–27] Using high frame-rate recording to avoid the cut-off in velocity magnitude, PIV can be used to differentiate flow structure from its first application in healthy individuals and patients with diastolic dysfunction.[28,29] Echo-PIV enables visualization of intraventricular vortex formation (Figure 3a) and monitoring of beat-by-beat variability.

A major limitation of echo-PIV is that blood velocities are shown only on 2D slices (scan plane) of the actual 3D flow, whereas 3D echocardiography has a largely insufficient space–time resolution to allow PIV processing. The extension of echocardiographic techniques to multiplanar echocardiographic acquisitions has demonstrated that reconstructing 3D blood flow motion might be possible (Figure 3b).[30]

An exploration of the properties of blood motion requires the evaluation of quantities related to the velocity gradient tensor, such as vorticity and energy dissipation.[31] Techniques to estimate velocity gradients based on PIV have been developed[32] and have been preliminarily applied to echo-PIV.[33] However, the spatial resolution of echo-PIV is still low, and might be insufficient for the smallest scales of (weakly) turbulent blood motion; quantification of blood motion based on gradients should, therefore, be interpreted with care. *In vivo* visualization of blood flow and flow-derived IVPG[17,33] parametric maps offer an opportunity to improve methods for the diagnosis, medical treatment, and surgical repair of cardiovascular disease.

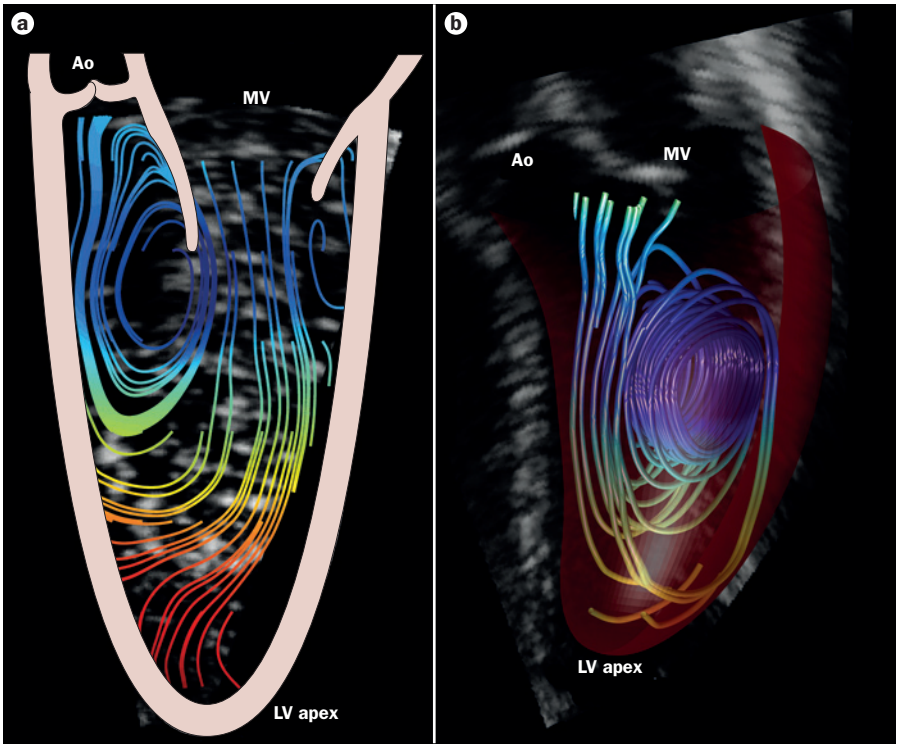

Figure 3 | Echocardiographic recordings of intraventricular swirling flow in healthy individuals. **a** | Streamlines during late diastolic filling. The vortex is visible behind the anterior mitral leaflet. **b** | 3D streamlines reconstructed from multiplane acquisition at the onset of systole. The streamlines spiral out from the vortex and are directed towards the outflow tract. In both images, pressure gradient is directed from apex to the base (in colour scale from red to blue). Minimal pressure is found at the centre of the vortex for centrifugal effect. Abbreviations: Ao, aorta; LV, left ventricular; MV, mitral valve.

Vortex analysis in LV disease

Although vortex analysis represents a new paradigm for investigating the functional properties of the heart, the pathophysiological relevance of cardiac fluid dynamics is still unknown and quantitative data are inconclusive. The first clinical studies on LV vortices were initiated as global indicators of vortex formation[34] and were followed by studies in animals during impaired electrical activation.[28] Investigation progressed to patients with dilated cardiomyopathy, in whom the geometrical properties of LV vortex were analysed.[29] Vortical properties, such as position and circulation (the amount of vorticity, or local fluid particle rotation,[14] contained inside the vortex), have been shown to be modified with disease, characterized by weakened and basal vortices. Research has also been focused on the transit properties of blood inside the left ventricle as an index of flow quality.[20] These techniques show that LV dilatation or dyskinesia give rise to a distorted and weakened vortex, local stagnation, and reduced flow exchange with an increased risk of thrombus formation.[22,35,36] These studies demonstrate intraventricular, fluid-dynamic phenomena associated with pathologies such as dilated cardiomyopathy and ischaemia, which had previously been detected using other diagnostic methods.[22,35,36]

The attempt to characterize pathological conditions in terms of LV flow properties is a step forward in diagnostic technology. The persistence of vortex circulation from early to late diastole delineates normal haemodynamic coupling between LV filling and emptying that seems to be lost in patients with nondilated heart failure.[37] Moreover, the timing of LV vortex formation is immediately modified by turning off a biventricular pacemaker in patients receiving cardiac resynchronization therapy, although changes in tissue dynamics could not be detected by available technology.[38]

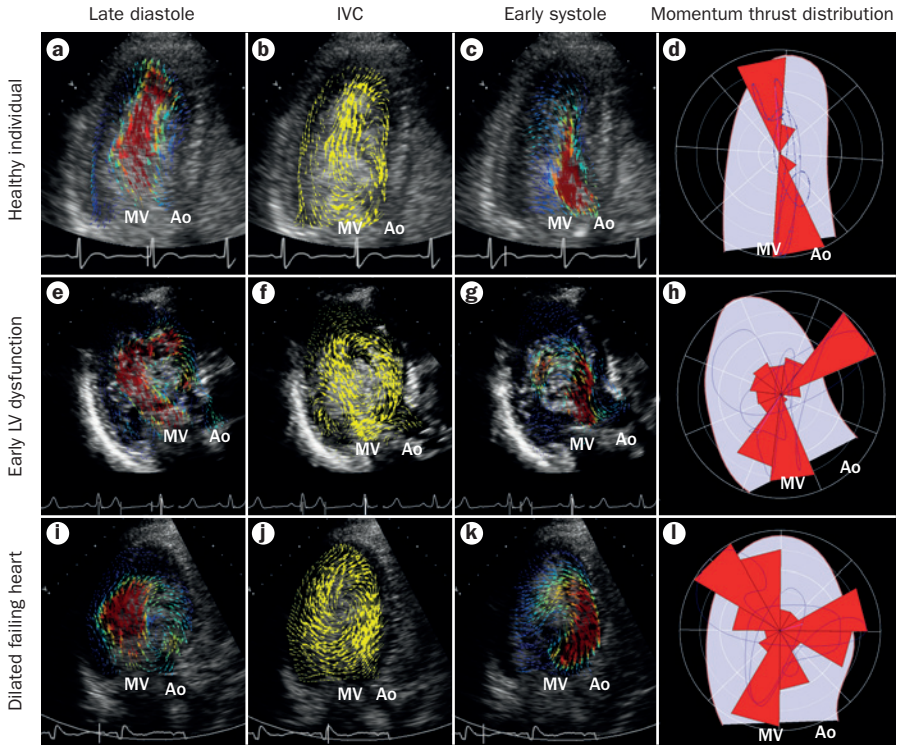

Figure 4 | Echocardiographic recordings of intraventricular flow. **a–d** | A healthy individual. **e–h** | A patient with subclinical diastolic dysfunction. **i–l** | A patient with dilated cardiomyopathy. Velocity vectors are shown at late diastole (parts a, e, and i), during IVC (parts b, f, and j), and in early systole (parts c, g, and k). Colours in late diastole and early systole represent kinetic energy (from blue to red), arrow lengths are amplified during low-velocity IVC. The polar histogram of the frequency and intensity of intraventricular forces is shown in parts d, h, and l. Momentum thrust is the integrated result of IVPG, and is composed of gradients of kinetic energy and flow acceleration representing the force acting on the entire mass of fluid. The observed base–apex or apex–base orientation of intraventricular forces perfectly matches with LV geometry, with a highly curved apex and rectilinear side walls, and ensures correct interaction between blood flow and myocardial tissue. Normal blood flow develops along the longitudinal axis in association with the filling–emptying mechanism. The longitudinal orientation is lost in the presence of early LV dysfunction, and the initiation of transversal forces might stimulate LV adaptation. At later stages of LV failure, the streamlines become rounded and the base–apex function is replaced by disorganized dynamic actions. Abbreviations: Ao, aorta; IVC, isovolumic contraction; IVPG, intraventricular pressure gradients; LV, left ventricular; MV, mitral valve.

These findings indicate that flow analysis can reveal small modifications in LV function before ventricular tissues have undergone changes in mechanical properties that are clinically relevant.

In healthy individuals, echo-PIV shows that diastolic mitral jets give rise to the formation of a vortex (Figure 4a–c), which is particularly visible during the volumetric slow-filling phase, diastasis, and especially during isovolumic contraction. This kinematic description of blood motion is associated with dynamic thrusts that are principally oriented along the base–apex direction to comply with the filling–emptying mechanism (Figure 4d). The normal vortex ensures a smooth transition from diastole to systole with apex-reaching blood streams and strictly longitudinal pressure gradients.

This harmonious and dynamic interaction between blood and tissue is disturbed in the presence of disease, with regional, mechanical, or electrical dyskinesia, loss of synchronicity, or abnormal ventricular geometry. Figure 4e–h shows a patient with diastolic dysfunction and preserved ejection fraction. Here, the forming vortex is less coherent and flow is more irregular (weakly turbulent) than in healthy individuals. The incoming jet is partly deviated, and ejection follows a curved path. Altered fluid dynamics give rise to the development of transversal forces and unnatural timing. In a patient with a dilated ventricle (Figure 4i–l), the flow follows curved streamlines that can be smooth and regular (as in this example) or more turbulent, resulting in intraventricular forces that have lost the facilitating longitudinal orientation.

Understanding of clinical outcomes related to intraventricular vortex dynamics is still limited. Further studies are required to characterize normal vortex properties and their age-related or exercise-related changes. Furthermore, systematic analysis of modifications in LV vorticity in the presence of carefully delineated pure pathologies, such as hypertrophic cardiomyopathy, myocardial infarction, and mitral valve diseases, or genetic malformations should be planned. We also need to consider appropriate metrics for the assessment of vorticity patterns and for blood momentum, both of which are indicative of the interaction between blood motion and the surrounding tissue.

The vortex in LV remodelling

LV remodelling describes the changes in ventricular architecture, including cavity shape and wall structure, which occur in response to abnormal loading conditions, or as a consequence of primary, acquired, or genetic myocardial diseases.[39] Starting as an adaptive mechanism triggered by injury, LV remodelling can become, in the absence of corrective interventions, a self-perpetuating maladaptive process towards myocardial deterioration and clinically overt heart failure. LV remodelling underlies a complex interplay of biomechanical and neurohumoral stress responses, culminating in hypertrophic gene activation and cell growth.[40–43] Although a factor in subsequent heart failure, LV remodelling can exhibit a variable phenotype in terms of hypertrophy and cavity dilatation, which is correlated with clinical outcomes.[44]

Although the full mechanisms of LV remodelling are not completely understood, a local increase in wall stress triggering a sequence of events that amplifies and extends the damage to the whole ventricle is considered the principal path leading to LV remodelling.[45] Clinical algorithms that consistently predict the risk of LV remodelling, before irreversible loss of the contractile filaments for accumulation of cytoskeletal proteins, are few and those that exist are rather primitive.[46–48] In the next two sections, we discuss the potential role of cardiac vortices in LV remodelling.

Tissue–blood flow interactions

Existing predictive models of LV remodelling focus on the myocardium, and do not consider the presence of blood vortical motion inside the cardiac chambers. The normal left ventricle exhibits a dynamic balance between contractile performance,

active aspiration, and elastic properties, with the spatial distribution of time-varying intraventricular forces that drive blood flow during the emptying–filling function. In other words, the natural interaction between fluid and tissue is slightly asynchronous in motion, perfectly matching the asymmetric vortex formation and laterally displaced inflow and outflow jets through longitudinal IVPG. Such a harmonious balance is, to varying degrees, corrupted in patients with a dysfunctional heart, but can also be substantially impaired well before the onset of LV remodelling in several clinical conditions (such as asynchronous LV contraction, suboptimal resynchronization therapy, or early LV diastolic dysfunction).

Blood is an incompressible medium with about the same weight as tissue, and every segment in a chamber of the heart is in touch with the other segments through the column of blood between them. Therefore, the transfer of momentum from one region of the left ventricle to another occurs through blood, and is modulated by its unsteady vortical motion that reflects, in terms of dynamic actions, the time-course of IVPG.

Disrupted LV fluid mechanics is characterized by two factors. First, poor energetic performance, with irregular shear fluctuating stress owing to vortex instability, resulting in a substantial increase in energy dissipation. Second, deviation of IVPG from the normal base–apex direction, owing to the deviation in vortex-driven flow. IVPG forces are transmitted from the LV walls to other segments through incompressible blood, and transversal IVPG during systole can be interpreted as thrust-provoking work carried out by the myocardium in a facing tissue element, rather than supporting the emptying process. Dysfunctional flow is also commonly associated with the presence of initial turbulence, so that each phenomenon is amplified by its long tail fluctuating characteristic. Such fluctuations have a high frequency and a high wave number, and are not detectable with commonly used diagnostic technology, such as PCMR or echocardiography, but act as an amplifier of the forces exchanged between blood and tissue.

In addition to underlying biological causes or local myocardial stress, the evolution of LV remodelling might be modulated by inappropriate adaptation mechanisms that cannot restore harmonious interaction between tissue and flow. In our opinion, formed on the basis of personal experience, the presence of abnormal intraventricular fluid dynamics indicates a nonphysiological interaction between blood flow and tissue characterized by increased energy loss, sharp turbulent fluctuation, and pressure hammering, giving rise to an increase in inappropriately timed sharp stress onto the LV walls. This altered flow is an 'unstable' condition that induces regional hypertrophy and stiffening, impairing smooth accompaniment of blood flow, and increasing transversal IPVG and turbulence. These factors, through structural and functional changes in the myocyte and nonmyocyte compartments (downregulation of contractile and sarcomeric skeleton proteins and upregulation of cytoskeletal proteins), increase wall stress and mechanical stretch of the myocytes leading to further imbalance. Therefore, regardless of the initial cardiac insult, ventricular dilatation can become a self-sustaining process of deterioration in LV structure and function, where progressive chamber enlargement becomes a stimulus for further hypertrophy and dilatation. The remodelling process is regulated and amplified by genetic and neurohormonal factors, but mainly by mechanical fluid-dynamic elements that trigger and perpetuate anatomical damage (Figure 5).

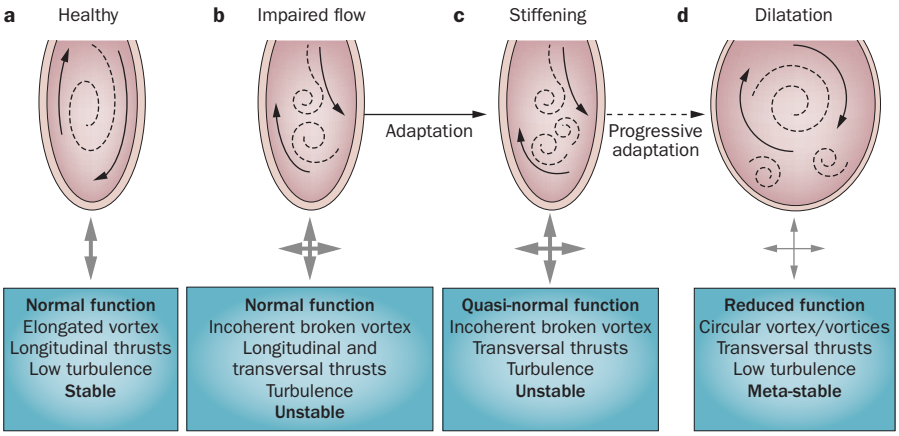

Figure 5 | The vortex in left ventricular remodelling. **a** | Healthy left ventricular function is a physiologically stable state, characterized by a smooth filling and emptying flow (black arrows) accompanied by a regular vortex (dashed line), which is associated with longitudinal intraventricular pressure gradients (grey arrows at bottom of image). **b** | Impaired flow, even in the presence of normal volumetric indices, is associated with transverse intraventricular pressure gradients and turbulent fluctuations, which translate into unnatural myocardial stress, inducing adaptations (unstable state). **c** | Early adaptation is often characterized by an increase in chamber stiffness that worsens the negative flow effect and induces further adaptation. **d** | The dilated left ventricle represents a 'meta-stable' state, meaning a state with reduced left ventricular function and unnatural mechanics that remains almost stable (or progresses slowly) owing to a limited capacity for further adaptation.

Epigenetic role of LV flow

In the past few years, epigenetic mechanisms, consisting of gene expression changes owing to interactions between the organism and the environment, have emerged as important modulators of cardiac disease.[49,50] Epigenetic modifications can trigger subclinical cardiac disorders and contribute to clinically overt cardiac pathologies. The vortex has an important role during the mbryogenic phase, triggering the biochemical pathways that activate some of the genes involved in morphological cardiovascular development (flow-guided model).[51] In the clinical setting, LV remodelling is commonly accompanied by reinduction of the fetal gene programme, mimicking the gene expression of embryonic development.[43,52] In this genetic adaptive contest, the interplay between tissue and blood flow might regain the fetal memory, corroborating some features of cardiac adaptive–maladaptive LV remodelling. Owing to the stress burden imposed on the myocardium, impaired LV fluid dynamics can be regarded as an environmental factor that facilitates varying gene expression or phenotype intensity of the same gene.[53]

The epigenetic role of flow has been demonstrated in models of vascular disease; however, no conclusive data exist for its role in cardiac disease.[53,54] In a small number of patients with dilated cardiomyopathy and mild LV remodelling, but with preserved stroke volume, an abnormal flow pattern was found using MRI, suggesting an early (subclinical) pathogenic role of intracardiac fluid-dynamic changes.[55] The analysis of epigenetic mechanisms related to fluid disturbance as potential co-factors in LV

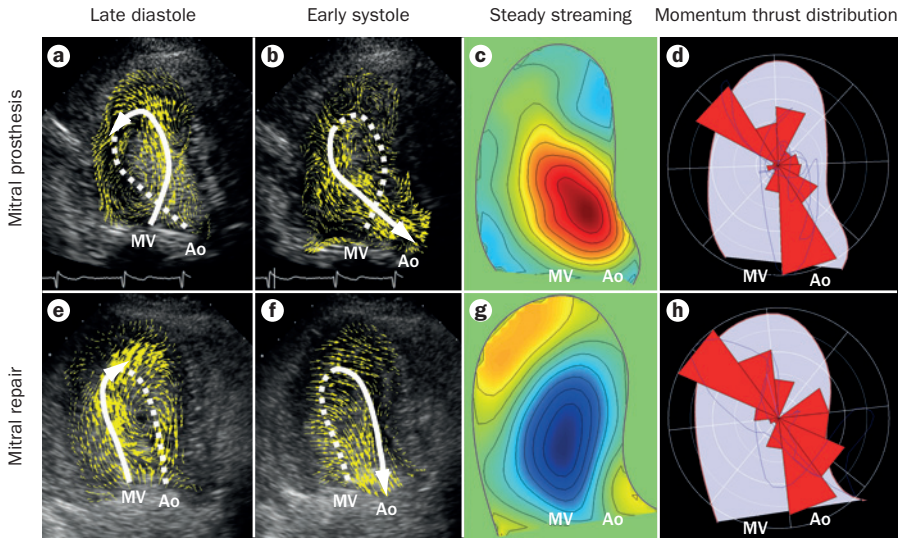

Figure 6 | Echocardiographic recordings of postsurgical intraventricular flow. **a**–**d** | Implantation of a mechanical bileaflet mitral valve. The flow after valve prosthesis implantation shows the inversion of the vortex rotation that gives rise to higher turbulence and disturbed flow. **e**–**h** | Mitral valve repair, with normal flow rotation maintained. Velocity vectors are shown at late diastole (parts a and e) and early systole (parts b and f). The thick white line is used to sketch the mean path of blood flow during the heart beat (the continuous line represents blood-flow direction and the broken line refers to a mirror image of the subsequent or previous cardiac phase). Colour maps (parts c and g) show the steady-streaming pattern (the net-flow averaged over one heart beat) in terms of vortex rotation intensity from red (anticlockwise) to blue (clockwise). The polar histogram of the frequency and intensity of intraventricular forces is shown in parts d and h. In both mitral valve replacement and repair, intraventricular forces show a mild deviation from the longitudinal direction. Abbreviations: Ao, aorta; MV, mitral valve.

remodelling, could stimulate corrective interventions in the early phase of disease to prevent advanced pathological phenotypes and adverse cardiovascular outcomes.

The vortex in cardiac surgery

Surgical treatment targeting the cause of haemodynamic cardiac overload can improve symptoms and survival rates.[56] Optimal timing and choice of surgical strategies are the main determinants of postoperative clinical results.[57,58] However, as well as targeting cardiac overload, surgical procedures should be aimed at preventing or reversing LV remodelling to attempt neutralization of heart disease. In addition to evaluating successful treatment of the cardiac lesion, intraoperative assessment of the correction or redevelopment of impaired blood flow might have an important role in the LV remodelling process and long-term surgical outcomes.

Despite successful lesion correction, impaired fluid dynamics can still be observed after mitral surgery. For example, reversed vortical motion has been documented in patients after prosthetic valve replacement,[59,60] with varying flow patterns depending on the type, orientation, and position of the valve prosthesis. The reversed vortical motion pattern is associated with a significant increase in energy dissipation and a modification of pressure distribution on the LV wall that deviates from the longitudinal orientation.[59,60] By contrast, we have noticed that preserving the native valve apparatus with mitral repair maintains normal flow rotation, avoiding the development of turbulence. Examples of flow after prosthetic valve replacement and mitral valve repair are shown in Figure 6. In both mitral valve replacement and repair, the distribution of intraventricular forces can deviate from the longitudinal direction, depending on the individual flow established after surgery. Therefore, mitral valve repair should be designed to treat valve lesions, achieving a physiological flow pattern to attempt the ultimate 'curative' effect.

Surgical ventricular reconstruction might be an effective therapy in selected patients with LV aneurysm or extensive scarring.[61,62] Reconstruction focused on LV shape, volume, and ejection fraction as functional end points lead to inconsistent results.[63] On the basis of MRI analysis, current surgical techniques have been found to affect the pattern of LV flow vortex with stagnation at the apex.[64] Although unexplored in the clinical setting, echo-PIV used instead of conventional volume-dependent parameters could guide surgeons to predict and optimize the flow characteristics of LV reconstruction procedures.

Assessment of the surgical quality is based on guidelines and experience, but a patient's response to surgery can be determined only during follow-up, after tissues have had time to readjust into a balanced state. Intraventricular flow analysis can be used to assess the quality of blood flow immediately after surgery, when maladaptive fluid dynamics are the preliminary indicator of suboptimal cardiac function and a high risk of adverse outcome. A natural flow with a regular, stable vortex and aligned IVPG is necessary, although not sufficient, for a positive outcome.

The vortex in device therapy

Animal models have shown that pathological conditions of the left ventricle associated with electromechanical asynchrony give rise to changes in the physiological time-course of regional IVPG.[65,66] Altered filling–empting dynamics determine pathological changes related to tissue stress, potentially triggering LV remodelling. For example, the inward diastolic movement of a dyskinetic segment can impart motion to blood pooled in other regions of the left ventricle, inducing local stress in remote segments. The loading time affects the onset and duration of relaxation. Thereby, the asynchrony or asynergy of a segment induces further mechanical disruption in remote segments, starting a spiral of progressive pumping inefficiency and flow derangement.

Cardiac resynchronization therapy with an implanted device can revert mechanical asynchrony and related LV dysfunction and remodelling in selected patients.[67,68] Figure 7 shows the changes in fluid dynamics in a patient who responded, with reverse remodelling, to cardiac resynchronization therapy (biventricular pacemaker).

Changes in fluid dynamics have been reported with 4D flow particle PCMR analysis in an animal model of mechanical LV epicardial assistance for myocardial infarction.[69] Unassisted cardiac beats revealed highly discoordinated flow towards the infarcted area, with several large signal voids, indicating a very slow or stagnant pattern of blood flow. Synchronized epicardial assistance induces dramatic regional and global flow improvements with a redistribution of stagnant blood towards the functioning remote myocardium. These flow changes are prominent during diastolic

device deflation, and minimal during systole, confirming the relevance of device-induced characteristics on fluid dynamics for more efficient ejection.[69]

Cardiac mechanical support with LV assist devices can be used in patients with advanced heart failure as 'a bridge to recovery',[70] offering an important clinical model for prospective evaluation of the interplay between tissue and blood flow in the reversal or redevelopment of LV remodelling. Mechanical cardiac unloading with LV assist devices can induce reverse remodelling, relieving the structural abnormalities of cardiomyocytes and extracellular matrix, which are correlated with the duration of mechanical unloading.[71–73] Although unexplored, the restoration of fluid dynamics, in addition to other parameters, might provide new criteria for the evaluation of sustained myocardial recovery and device explantation. These perspectives should inspire further research to better understand the mechanisms involved in both myocardial remodelling and its regression in the setting of surgical and device therapy.

Conclusions

In addition to the conventional parameters of LV function, the analysis of fluid dynamics provides new insight into the complex haemodynamic burden of cardiac disease. The vortex can be seen as a sensitive harbinger of subsequent maladaptive LV response, guiding therapeutic strategy with the hope of achieving optimal cardiovascular outcome. Future studies and research programmes on the epigenetic role of cardiac fluid dynamics might signal an early understanding of the LV remodelling spectrum and target new therapeutic strategies to prevent congestive heart failure.

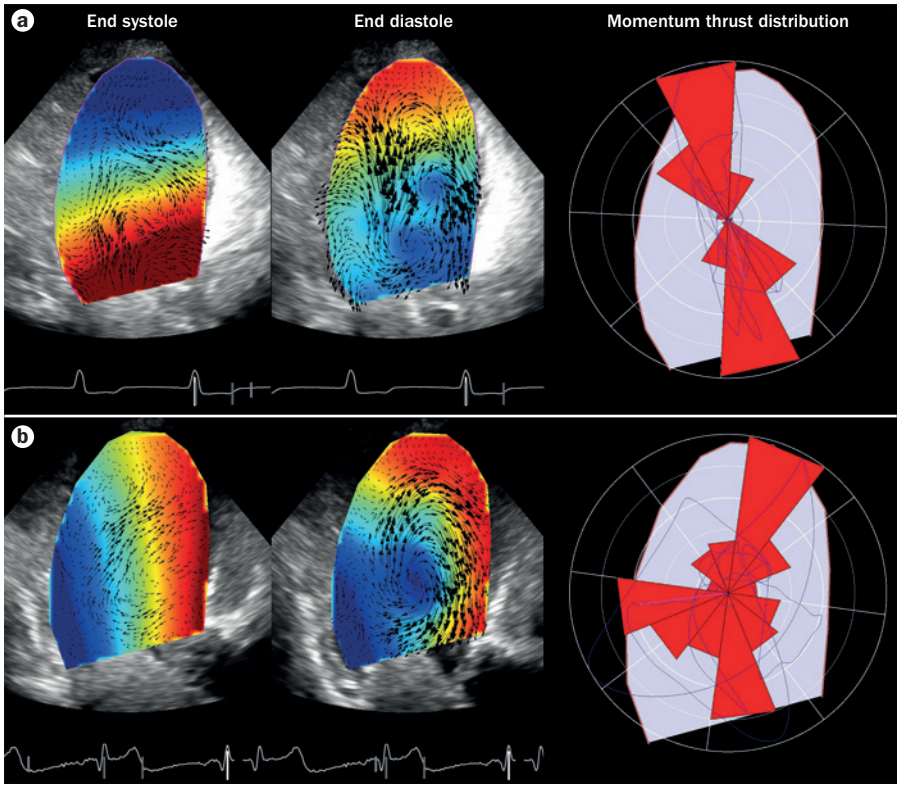

Figure 7 | Longitudinally directed intraventricular pressure gradients are markers of normal left ventricular function. Echocardiographic recordings from a patient who responded, with reverse remodelling, to cardiac resynchronization therapy (biventricular pacemaker). **a** | Under normal conditions (pacemaker on), the various segments of the left ventricle are physiologically dyssynchronous. Their lack of homogeneity in space and time bears longitudinal pressure gradients inside an asymmetric cavity with its individual shape dimensions, and transmural stresses. Normal flow develops base-to-apex suction at the onset of diastole and apex-to-base thrust at the onset of systole. **b** | A few heart beats after pacing deactivation (pacemaker off), small differences in segmental mechanics are associated with nonphysiological blood motion with the onset of transversal pressure gradients. Diastolic filling impacts on lateral segments and regional systolic contraction provokes thrust on facing walls. Altered filling–emptying dynamics give rise to pathological changes in space–time occurrence of tissue stresses, possibly triggering the loop of LV remodelling. Red indicates high pressure and blue indicates low pressure.

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Author contributions
All the authors researched data for the article, discussed its content, wrote the manuscript, and reviewed/edited it before submission.

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